Arg3.1 plays a pivotal role in the late phase of LTP and the consolidation of LTM

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Enduring forms of synaptic plasticity require alterations in the molecular composition and structure of neurons and are dependent on RNA and protein synthesis. Functional plasticity might therefore be achieved by activity-dependent changes in the expression of specific genes. The expression of Arg3.1 is robustly induced by LTP stimulation. Moreover, following induction Arg3.1 mRNA and protein are rapidly distributed throughout the dendritic arbor and can be specifically targeted to stimulated synapses. Here, Arg3.1 protein is embedded into the postsynaptic density and is associated with the NMDA receptor complex. This association is mediated by PSD95, a protein that can directly bind to the NMDAR. We have generated Arg3.1 knockout mice. These animals exhibit a remarkable biphasic alteration of hippocampal LTP. Whereas baseline synaptic transmission is normal the early phase of LTP is enlarged. However, elevated potentials completely decay to baseline and no late phase LTP can be observed. Arg3.1 mutant mice were further tested in various behavioral learning and memory tasks. In the Morris water maze knockout mice show a weaker learning performance during acquisition and a dramatic impairment in memory consolidation. During classical fear conditioning formation of both cue and context dependent long term memory are impaired in Arg3.1 mutant mice and in conditioned taste aversion knockout animals fail to form a stable memory for the association of taste and malaise. Thus, Arg3.1 may act to maintain the structural or functional integrity of the NMDAR complex and thereby control the signaling pathways that coordinate activity-dependent changes underlying long-lasting synaptic plasticity and memory storage.